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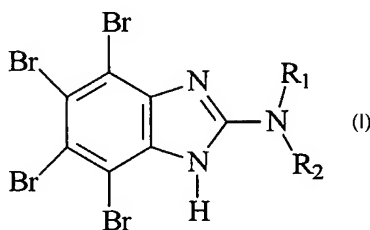
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(54) Title: NEW DERIVATIVES OF 4, 5, 6, 7-TETRABROMOBENZIMIDAZOLE AND METHOD OF THEIR PREPARATION



(57) Abstract: New derivatives of 4, 5, 6, 7-tetrabromobenzimidazole of formula (I); wherein R₁ is hydrogen or aliphatic group, R₂ is aliphatic group optionally substituted with hydrogen or substituent such as hydroxyl group or substituted amino group and method of their preparation.

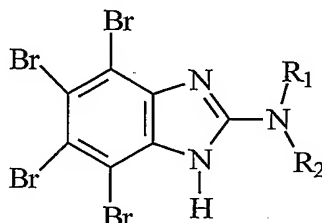


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AMENDED CLAIMS

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original claims 1-21 replaced by amended claims 1-21 (2 pages)]

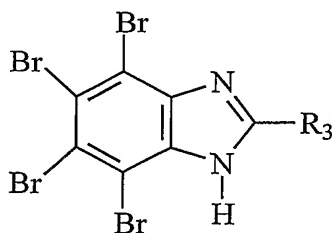
1. New derivatives of 4,5,6,7-tetrabromobenzimidazole of formula 1



Formula 1

wherein R₁ is hydrogen or methyl group, R₂ is (C₁-C₃)aliphatic group or (C₁-C₃)aliphatic group substituted at the position 2 with hydroxyl or dimethylamino group.

2. A new derivative according to Claim 1, which is 2-methylamino-4,5,6,7-tetrabromo-1H-benzimidazole.
3. A new derivative according to Claim 1, which is 2-dimethylamino-4,5,6,7-tetrabromo-1H-benzimidazole.
4. A new derivative according to Claim 1, which is 2-ethanolamino-4,5,6,7-tetrabromo-1H-benzimidazole.
5. A new derivative according to Claim 1, which is 2-isopropylamino-4,5,6,7-tetrabromo-1H-benzimidazole.
6. A new derivative according to Claim 1, which is 2-(2-hydroxypropylamino)-4,5,6,7-tetrabromo-1H-benzimidazole.
7. A new derivative according to Claim 1, which is 2-(2-dimethylaminoethylamino)-4,5,6,7-tetrabromo-1H-benzimidazole.
8. A method of preparation of new derivatives of 4,5,6,7-tetrabromobenzimidazole of formula 1, wherein R₁ is hydrogen or methyl group, R₂ is (C₁-C₃)aliphatic group or (C₁-C₃)aliphatic group substituted at the position 2 with hydroxyl or dimethylamino group in the reaction of the compound of formula 2,



Formula 2

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wherein the substituent R₃ is halogen, alkylthio group or lower alkoxy group or other group easily being substituted, with an amine, at elevated temperature, and then the resulting product is purified by crystallization or chromatography on silica gel.

9. The method according to Claim 8 wherein in the compound of formula 2, the substituent R₃ is halogen consisting of Cl or Br, or alkylthio group consisting of CH₃S, C₂H₅S, C₃H₇S, or (C₁-C₃)alkoxy group consisting of CH₃O, C₂H₅O or other group easily being substituted consisting of (C₁-C₃)alkylsulfone group or (C₁-C₃)alkylsulfoxide group.
10. The method according to Claim 8 wherein as the amine, a primary (C₁-C₃)aliphatic amine is used.
11. The method according to Claim 10 wherein the primary (C₁-C₃)aliphatic amine includes in the aliphatic chain additionally hydroxyl groups or dimethylamino group.
12. The method according to Claim 8 wherein as the amine, a secondary (C₁-C₃)aliphatic amine is used.
13. The method according to Claim 8 wherein the amine is used both as a reagent and a solvent in an aqueous or alcoholic solution.
14. The method according to Claim 8 wherein the reaction of the compound of formula 2 with the amine is carried out within the temperature range from 80 to 140 °C.
15. The method according to Claim 8 wherein the compounds of formula 1 can be converted by a known method into salts of mineral or organic acids.
16. A pharmaceutical composition exhibiting anti-neoplastic activity, containing effective anti-neoplastic acting amount of the compound according to Claim 1, combined with at least one inert, pharmaceutically acceptable carrier or diluent.
17. A pharmaceutical composition exhibiting anti-neoplastic activity, containing effective, anti-neoplastic acting amount of the compound according to any one of Claims 2 - 7, combined with at least one inert, pharmaceutically acceptable carrier or diluent.
18. Use of new derivatives according to Claim 1 for manufacturing of a drug having anti-neoplastic activity.
19. Use of new derivatives according to any of the Claims 2 - 7 for manufacturing of a drug having anti-neoplastic activity.
20. A method of inhibiting caseine kinase activity 2 in patients in need of such treatment by administration of effective amount of the compound of formula 1 according to Claim 1.
21. A method of inhibiting caseine kinase activity 2 in patients in need of such treatment by administration of effective amount of the compound of formula 1 according to any of the Claims 2-7.